

REMARKS

I. Status of the Claims

Claims 1-29 were pending and were subject to restriction and election requirements. Claims 1-8 and 10-29 stand rejected under 35 U.S.C. § 103(a). Claim 9 has been withdrawn from consideration subject to the restriction and election requirements. Applicants respectfully request that claim 9 be reconsidered upon the allowance of the pending claims.

II. Rejections Under 35 U.S.C. § 103(a)

The Office rejects claims 1-8 and 10-29 as allegedly prima facie obvious over the teachings of U.S. Pat. No. 6,087,509 (Claussner-'509) or U.S. Pat. No. 5,750,553 (Claussner-'553) in view of U.S. Pat. No. 5,558,859 (Cretois), in further view of U.S. Pat. No. 5,916,910 (Lai), U.S. Pat. No. 5,541,220 (Ismail), WO 92/21317 (Galey), WO 91/19701 (Dumats), and EP 427 625 (Estradier). See Office Action at 2-3. The Office admits that neither Claussner-'509 nor Claussner-'553 "teach[es] preferred [(A)] film forming agents, [(B)] solvents, [(C)] plasticizers and additives." See Office Action at 4. The Office, nevertheless, urges that "[i]t would have been obvious to one of ordinary skill in the art ... to modify the compositions of [either Claussner-'509 or Claussner-'553] by using the teachings of [Cretois] and obtain a composition comprising [(D) a compound of] formula (I), vinylimidazolium methochloride/vinylpyrrolidone copolymer [(a species of (A))], polyethoxylated hydrogenated castor oil [(a species of (C))], and solvent [(B)]." See Office Action at 5.

The rejection is improper because there is no motivation to combine and/or to modify the teachings of the references. The Office has merely used Applicants' specification as a hindsight road map to recreate the claimed invention. To prevent the use of hindsight, "[t]he initial burden is on the examiner to provide some suggestion of the desirability of doing what the inventor has done." See *M.P.E.P.* § 2142. That has not been done in this case.

A. The Office has failed to provide any basis for the desirability of the claimed combination.

"The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination." *M.P.E.P.* § 2143.01 (emphasis in original). The alleged motivation is listed on pages 5 or 6. However, these listed items merely identify ingredients or forms of a composition. For example, item b) is "[Cretois] teaches antiseborrheic agents" and item c) is "[Claussner-'509 and Claussner-'553] teach compositions comprising [a compound of] formula (I) for the treatment of hyperseborrhea." See Office Action at 5-6. Conspicuously absent from the alleged motivation is any desirable reason to choose the specifically proposed ingredients (A) to (D) from the disparate references to form a single composition within the scope of the claims.

At best, all that has been shown is that each ingredient of the claimed invention can be found in at least one of the seven cited references. Yet a prima facie case of obviousness requires a basis for the desirability of, or in other words the motivation for, the proposed combination. *M.P.E.P.* § 2143.01-02. In this case,

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the Office has yet to identify any desirable reason, i.e., motivation, to bring each of the proposed ingredients together into a single composition of either Claussner-'509 or Claussner-'553.

A motivation to combine teachings of various references cannot be established by merely implying one of ordinary skill in the art is capable of creating the claimed invention from bits and pieces of the documents of record. See *M.P.E.P.* § 2143.01. Nor can the motivation be established by discussing how the teachings of the references may allegedly be combined. See *M.P.E.P.* § 2143.01. Identifying ingredients and forms within the teachings of references cannot be equated with a motivation to combine those teachings. Because the Office failed to provide any basis for the desirability of the claimed combination, the rejection is improper. The rejection should be withdrawn for this reason alone.

B. The Office has failed to show where the references provide the motivation.

The motivation must be found in the prior art. See *M.P.E.P.* § 2143.01. The Office admits that neither Claussner-'509 nor Claussner-'553 teaches the preferred film forming agents, solvents, and plasticizers. Lai, Ismail, Galey, Dumats, and Estradier were not used to remedy these deficiencies in Claussner-'509 or Claussner-'553.

Only Cretois was cited to remedy the deficiencies of Claussner-'509 or Claussner-'553. At most, Cretois teaches antisebberhoieic agents, but the disclosure of a genus does not necessarily render each species within that genus *prima facie* obvious. See *In re Jones*, 21 U.S.P.Q.2d 1941 (Fed. Cir. 1992). The

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genus of antiseborrhoeic agents is too large to inherently describe every member within it. *Cf. M.P.E.P.* § 2144.08 II. A 4 a. "Some motivation to select the claimed species or subgenus must be taught by the prior art." *Id.* Yet Cretois fails to identify any antiseborrhoeic specie. The silence of Cretois cannot provide a motivation to select any particular specie, let alone the combination of all of the various ingredients from seven different sources in order to obtain the claimed composition. Again, for this reason alone, the rejection should be withdrawn.

C. The Office has failed to explain why the combination of the teachings is proper.

"When the motivation to combine the teachings of the references is not immediately apparent, it is the duty of the examiner to explain why the combination of the teachings is proper." *M.P.E.P.* § 2142. Both Claussner-'509 and Claussner-'553 teach pharmaceutical compositions. Claussner-'509, col. 9, ll. 19-22; Claussner-'553, col. 13, ll. 52-55. On the other hand, Cretois teaches compositions for imparting good shape-retention to the hair, e.g., styling mousses, hair-setting lotions, and mascaras. Cretois, col. 1, ll. 25-27. What would motivate one of ordinary skill in the art to combine ingredients in a pharmaceutical composition with ingredients in a styling mousse, hair-setting lotion, or mascara? The record provides no answer.

Indeed, the Office has failed to explain why one skilled in the art would combine the teachings of the other references with the teachings of Claussner-'509, Claussner-'553, and Cretois. Merely acknowledging that additives of Lai, Ismail, Estradier, Galey, and Dumats may be added does not provide the required

motivation to establish a prima facie case to combine the teachings of the disparate references. Thus, the rejection is improper and should be withdrawn.

D. The proposed combination is contrary to accepted wisdom of the art.

"The totality of the prior art must be considered, and proceeding contrary to accepted wisdom in the art is evidence of nonobviousness." *M.P.E.P.* § 2145 X. D 3, citing *In re Hedges*, 228 U.S.P.Q. 685 (Fed. Cir. 1986). For example, known disadvantages in old products would naturally discourage a search for new inventions. See *id.*; *U.S. v. Adams*, 383 U.S. 39, 52, 148 U.S.P.Q. 479, 484 (1966). Specifically, the prior art of record discourages administration of antiandrogen drugs via the ineffective topical route for the treatment of seborrhea, by teaching that antiandrogens must be localized below the skin in the sebaceous gland to have a chance of inhibiting androgens.

Seborrhea is the excessive production of sebum. See, e.g., *The Science of Hair Care* at 469 (C. Zviak, ed. Marcel Dekker, Inc., New York (1986)) (submitted for consideration with the papers filed 8/16/01). Natural sebum exists within the sebaceous gland. *Id.* at 471. The sebaceous glands exist below the epidermis (outer skin) in the middermis. *Id.* at 476, Figure 3b. Sebaceous glands are stimulated mainly by androgens. *Id.* at 476. Androgens are locally active, i.e., an androgen will stimulate only the sebaceous gland in its location. See *id.*

For example, the *Science of Hair Care* hypothesizes the androgen (i.e., testosterone) penetrates the sebaceous gland of males thereby initiating a series of conversions, including (1) converting testosterone to DHT by 5- α -reductase and (2)

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binding DHT to DHT-sensitive receptors. *Id.* Such androgen induced overstimulation of the sebaceous glands may be inhibited, in theory, by targeting (1) and/or (2) with antiandrogens. See, e.g., *Specification*, p. 2, ll. 22-23. Anti-androgenic activity is present in the compounds of the Claussner-'509 and Claussner-'553 patents: "The products which are a subject of the present invention possess useful pharmacological properties, in particular they fix on the androgen receptor and they present an anti-androgenic activity." Claussner-'509, col. 9, ll. 19-22; Claussner-'553, col. 13, ll. 52-55.

Yet administering antiandrogens via topical routes has been disappointing due to the location of the sebaceous glands below the skin and the topography of the skin itself. *Science of Hair Care*, supra. at 490. The disappointment suggests the deeper location of the sebaceous gland in humans makes topical/local treatment ineffective. *Id.* Even if the antiandrogen were to pass the epidermal barrier of the skin, it still may encounter a stream of interstitial spaces in the upper dermis that will block the route to the sebaceous gland. *Id.* at 490-1.

Regardless of the mechanism, if topical formulations of antiandrogen drugs such as those of Claussner-'509 and Claussner-'553 have been discouraged in the art then formulating a topical antiandrogenic drug would be contrary to accepted wisdom. These topical formulations have known disadvantages due to the physiology of the sebaceous glands and its vicinity. These disadvantages would have naturally discouraged a search for new topical formulations.

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As a result, one of ordinary skill in the art would not have been motivated to use any antiandrogen, such as those of Claussner-'509 and Claussner-'553, in a topical formulation.

CONCLUSION

Applicants respectfully request reconsideration and reexamination of the pending claims. The Office is invited to contact Sean A. Passino at (202) 408-6065 if there are any questions that can be resolved by a telephone conference.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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By: _____



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